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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/001,755	10/24/2001	Peter William Taylor	4-20251C/C1C1/MA2102	5831

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THOMAS HOXIE  
NOVARTIS, CORPORATE INTELLECTUAL PROPERTY  
ONE HEALTH PLAZA 430/2  
EAST HANOVER, NJ 07936-1080

EXAMINER

YAEN, CHRISTOPHER H

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 11/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application N .

10/001,755

Applicant(s)

TAYLOR ET AL.

Examiner

Christopher H Yaen

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 26 September 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 22-34 is/are pending in the application.
- 4a) Of the above claim(s) 34 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 22-33 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

## **DETAILED ACTION**

### ***Election/Restrictions***

1. Applicant's election with traverse of group I in Paper No. 7 is acknowledged. The traversal is on the ground(s) that the restriction requirement was improper. This is not found persuasive because the product claimed (group I) and the method making the product (group II) are classified in different classes and subclasses thereby warranting a distinct search which is neither overlapping nor co-extensive. Multiple searches in different databases are needed to determine patentability over the prior art.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 22-34 are pending, claim 34 is withdrawn from further consideration as being drawn to a non-elected subject matter.
3. Claims 22-33 are examined on the merits.

### ***Information Disclosure Statement***

4. The Information Disclosure Statement filed 02/12/2002 (paper no. 4) is acknowledged and considered. A signed copy of the IDS is attached hereto.

### ***Claim Rejections - 35 USC § 112, 2<sup>nd</sup> paragraph***

5. Claims 22-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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6. With regard to claim 22, 23 and dependent claims thereof in the recitation of the terms "B/D" and or "BDBB", these are indefinite and unclear because the term are considered laboratory designated terms of which differ from laboratory to laboratory. Applicant must clarify or distinctly define what is intended by these terms. Currently, "B/D" and "BDBB" are terms of which carries no distinguishing features that help in defining its structure and or function.

***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 22-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fidler et al (EP 0 331635A2, 1989, IDS AA) in view of Weiner *et al* (WO 91/01719).

The claims are drawn to a pharmaceutical composition comprising an  $\alpha$ -interferon B/D hybrid contained in a liposome mixture comprises 50-75 mol %, 20-40 mol % and 5-10 mol % of neutrally charged, cholesterol, and negatively charged phospholipids, respectively (claim 22); wherein the  $\alpha$ -interferon B/D hybrid is  $\alpha$ -interferon BDBB (claim 23), wherein the neutrally charged phospholipid comprises at least one phosphatidylcholine (PC) (claim 24), dimyristoyl PC (DMPC) or a mixture of DMPC and PC (claim 25), wherein the negatively charged phospholipid comprises phosphatidylserine (PS) (claim 26), or dioleoyl phosphatidylserine (claim 27); wherein

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the lipid mixture is 55-70 mol %, 25-36 mol %, and 5-10 mol % of neutral, cholesterol, and negatively charged phospholipid respectively (claim 28); wherein the molar ratio is 9:5:1::neutral:cholesterol:negatively charged phospholipid (claim 29); wherein the liposomes have an average size of up to 200 nm (claim 30), and 80-180 nm (claim 31); wherein the weight ratio of  $\alpha$ -interferon B/D hybrid to lipid mixture is 1:400 to 1:300 (claim 32); and wherein the liposome is in dehydrated form (claim 33).

Fidler *et al* teach the use of the  $\alpha$ -interferon B/D or BDBB hybrids in a liposome preparation in the treatment of bladder carcinomas, as well the use of  $\alpha$ -interferon as a potent antiviral agent. Fidler *et al* also teaches the use of PC and PS that can be included to make the liposomes that meet the limitations of the instant claims (see page 11). Fidler *et al* also teaches that the ratio of the liposome to  $\alpha$ -interferon can be within the range of 1:300-400 (see page 5). Weiner *et al* makes up the deficiencies of Fidler *et al* by disclosing the specific ratios of liposome mixed together, the size of the liposomes, and the form of liposomes.

Weiner *et al* teach the delivery of interferons in a liposome composition that comprises a range of 1:0.5:0.01 to 3:3:1 of neutral:cholesterol:negatively charged phospholipids (see page 15). It is also disclosed that the phospholipid can be amongst DMPC, PS, PC, and cholesterol (see page 13, -15). Weiner *et al* also teach that size, charge and lipid composition is critical to ensure optimal entrapment (see page 14). It is disclosed that the minimum size of the liposomes can be 100nm (page 40) and that the liposome can be in dehydrated form (see page 17).

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It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to make a liposomal composition that will be useful for slow release of drug compounds in a subject, wherein the drug is  $\alpha$ -interferon B/D and BDBB hybrids. One of skill in the art would have been motivated to do so because Fidler *et al* taught that the combination of  $\alpha$ -interferon hybrids (i.e. B/D and BDBB) trapped within the specific liposomal mixtures was effective in the slow release and distribution of  $\alpha$ -interferon hybrids. One of skill in the art would have been motivated to do so in view of the teachings of the above references that one could expect a reasonable level of success in administering liposome entrapped interferons into a subject. The art accepted effect of interferon being an anti-viral agent and the fact that Fidler *et al* were able to deliver the interferon entrapped liposomes to treat bladder cancer would make it obvious that viral liver disease could also be treated with a good chance of success. Weiner *et al* taught the specific mixtures and ratios of different liposomes, size and charge of the liposomal composition were critical for the effective release, entrapment and stability of the composition. Therefore, one of ordinary skill in the art would have a reasonable expectation of success in modifying and or changing the composition of the lipids so as to achieve optimal entrapment, release, and stability.

### ***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

*Christopher Yaen for:*

Christopher Yaen  
Art Unit 1642  
October 22, 2003